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(54) **SILVER NANOPATE COMPOSITIONS AND METHODS**

(56) **References Cited**

U.S. PATENT DOCUMENTS

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4,526,698 A 7/1985 Kuroda et al.
5,226,907 A 7/1993 Tankovich

(Continued)

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FOREIGN PATENT DOCUMENTS

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DE 3905167 8/1989
DE 4344141 7/1995

(Continued)

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OTHER PUBLICATIONS

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Dierickx, et al. "Photodynamic Therapy for Nevus Sebaceus With Topical d-Aminolevulinic Acid", Arch Dermatol, vol. 135, Jun. 1993, pp. 637-640.

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(57) **ABSTRACT**

Embodiments of the present invention relate to methods for preparing high optical density solutions of nanoplates, such as silver nanoplates or silver platelet nanoparticles, and to nanoparticles, solutions and substrates prepared by said methods. The process can include the addition of stabilizing agents (e.g., chemical or biological agents bound or otherwise linked to the nanoparticle surface) that stabilize the nanoparticle before, during, and/or after concentration, thereby allowing for the production of a stable, high optical density solution of silver nanoplates. The process can also include increasing the concentration of silver nanoplates within the solution, and thus increasing the solution optical density.

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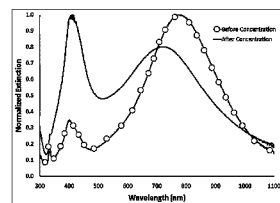
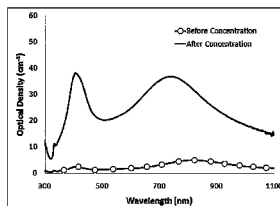
CPC **C09D 139/06** (2013.01); **A61K 9/5115** (2013.01); **A61K 9/5123** (2013.01); **A61K 9/5138** (2013.01); **A61K 33/38** (2013.01); **A61L 27/00** (2013.01); **B22F 1/0081** (2013.01);
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(58) **Field of Classification Search**

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B22F 1/0081; B22F 1/02; B22F 1/055;
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20 Claims, 4 Drawing Sheets



| | | | | | | |
|------|-------------------------|--|--------------|----|---------|--------------------|
| (51) | Int. Cl. | | 6,663,658 | B1 | 12/2003 | Kollias et al. |
| | <i>A61K 33/38</i> | (2006.01) | 6,676,655 | B2 | 1/2004 | McDaniel |
| | <i>A61L 27/00</i> | (2006.01) | 6,685,730 | B2 | 2/2004 | West et al. |
| | <i>B22F 1/00</i> | (2006.01) | 6,685,927 | B2 | 2/2004 | Sumian et al. |
| | <i>C09D 125/06</i> | (2006.01) | 6,685,986 | B2 | 2/2004 | Oldenburg et al. |
| | <i>C09D 129/04</i> | (2006.01) | 6,692,755 | B2 | 2/2004 | Gers-Barlag et al. |
| (52) | U.S. Cl. | | 6,699,724 | B1 | 3/2004 | West et al. |
| | <i>B22F 1/02</i> | (2006.01) | 6,706,032 | B2 | 3/2004 | Weaver et al. |
| | CPC | <i>C09D125/06</i> (2013.01); <i>C09D 129/04</i> | 6,720,006 | B2 | 4/2004 | Hanke et al. |
| | | (2013.01); <i>A61L 2300/104</i> (2013.01); <i>B22F</i> | 6,767,547 | B2 | 7/2004 | Gers-Barlag et al. |
| | | <i>1/0022</i> (2013.01); <i>B22F 1/0055</i> (2013.01); | 6,793,913 | B2 | 9/2004 | Tournilhac et al. |
| | | <i>B22F 1/02</i> (2013.01) | 6,800,122 | B2 | 10/2004 | Anderson et al. |
| (56) | References Cited | | 6,803,049 | B2 | 10/2004 | Gers-Barlag et al. |
| | U.S. PATENT DOCUMENTS | | 6,811,770 | B2 | 11/2004 | Ferrari et al. |
| | 5,409,797 | A 4/1995 Hosoi et al. | 6,814,760 | B2 | 11/2004 | Anderson et al. |
| | 5,423,337 | A 6/1995 Ahlert et al. | 6,821,509 | B2 | 11/2004 | Soane et al. |
| | 5,423,803 | A 6/1995 Tankovich et al. | 6,838,088 | B2 | 1/2005 | Gers-Barlag et al. |
| | 5,425,728 | A 6/1995 Tankovich | 6,852,252 | B2 | 2/2005 | Halas et al. |
| | 5,553,630 | A 9/1996 Dupuis et al. | 6,881,249 | B2 | 4/2005 | Anderson et al. |
| | 5,593,680 | A 1/1997 Bara et al. | 6,897,238 | B2 | 5/2005 | Anderson |
| | 5,647,866 | A 7/1997 Zaias et al. | 6,942,878 | B2 | 9/2005 | Ishii et al. |
| | 5,695,747 | A 12/1997 Forestier et al. | 6,955,639 | B2 | 10/2005 | Hainfeld et al. |
| | 5,713,845 | A 2/1998 Tankovich | 6,989,151 | B2 | 1/2006 | Gers-Barlag et al. |
| | 5,750,120 | A 5/1998 Miguel-Colombel | 7,018,396 | B2 | 3/2006 | Sierra et al. |
| | 5,752,949 | A 5/1998 Tankovich et al. | 7,037,513 | B1 | 5/2006 | Traynor et al. |
| | 5,756,110 | A 5/1998 Allard et al. | 7,131,446 | B2 | 11/2006 | Tang et al. |
| | 5,776,440 | A 7/1998 Forestier et al. | 7,144,627 | B2 | 12/2006 | Halas et al. |
| | 5,814,311 | A 9/1998 Le Bras-Roulier et al. | 7,201,765 | B2 | 4/2007 | McDaniel |
| | 5,817,089 | A 10/1998 Tankovich et al. | 7,270,721 | B2 | 9/2007 | Hilfenhaus et al. |
| | 5,830,177 | A 11/1998 Li et al. | 7,367,934 | B2 | 5/2008 | Hainfeld et al. |
| | 5,858,381 | A 1/1999 Le Bras et al. | 7,371,457 | B2 | 5/2008 | Oldenburg et al. |
| | 5,863,522 | A 1/1999 Forestier et al. | 7,435,524 | B2 | 10/2008 | Anderson et al. |
| | 5,925,035 | A 7/1999 Tankovich | 7,462,496 | B2 | 12/2008 | Malak |
| | 5,955,091 | A 9/1999 Hansenne | 7,494,503 | B2 | 2/2009 | McDaniel |
| | 5,958,389 | A 9/1999 Le Bras-Roulier et al. | 7,530,940 | B2 | 5/2009 | Hainfeld et al. |
| | 5,985,300 | A 11/1999 Crotty et al. | 7,648,595 | B2 | 1/2010 | Jin et al. |
| | 6,004,567 | A 12/1999 Marchi-Lemann et al. | 7,659,301 | B2 | 2/2010 | Anderson |
| | 6,036,684 | A 3/2000 Tankovich et al. | 7,704,754 | B2 | 4/2010 | Malak |
| | 6,050,990 | A 4/2000 Tankovich et al. | 7,758,561 | B2 | 7/2010 | Eppstein |
| | 6,060,041 | A 5/2000 Candau et al. | 7,758,888 | B2 | 7/2010 | Lapidot et al. |
| | 6,063,074 | A 5/2000 Tankovich | 7,776,130 | B2 | 8/2010 | Mirkin et al. |
| | 6,080,127 | A 6/2000 Li et al. | 7,780,955 | B2 | 8/2010 | Cassin |
| | 6,132,392 | A 10/2000 Stone | 7,785,623 | B2 | 8/2010 | Keller |
| | 6,132,745 | A 10/2000 Marchi-Lemann et al. | 7,790,066 | B2 | 9/2010 | Wang et al. |
| | 6,147,982 | A 11/2000 Sourour et al. | 7,829,073 | B2 | 11/2010 | Martin et al. |
| | 6,152,917 | A 11/2000 Tankovich | 7,959,624 | B2 | 6/2011 | Riesinger |
| | 6,168,590 | B1 1/2001 Neev | 8,033,977 | B2 | 10/2011 | Hainfeld et al. |
| | 6,183,728 | B1 2/2001 Forestier et al. | 8,057,418 | B2 | 11/2011 | Korbling et al. |
| | 6,183,773 | B1 2/2001 Anderson | 8,062,701 | B2 | 11/2011 | McClure et al. |
| | 6,235,270 | B1 5/2001 Ishii et al. | 8,178,202 | B2 | 5/2012 | Halas et al. |
| | 6,238,650 | B1 5/2001 Lapidot et al. | 8,182,786 | B2 | 5/2012 | O'Brien et al. |
| | 6,267,771 | B1 7/2001 Tankovich et al. | 8,197,471 | B1 | 6/2012 | Tersigni |
| | 6,283,956 | B1 9/2001 McDaniel | 8,268,332 | B2 | 9/2012 | Manstein |
| | 6,287,549 | B1 9/2001 Sumian et al. | 8,268,638 | B2 | 9/2012 | Stein et al. |
| | 6,333,026 | B1 12/2001 Lemann | 8,377,427 | B2 | 2/2013 | Giroud et al. |
| | 6,344,050 | B1 2/2002 Chen | 8,420,062 | B2 | 4/2013 | Josso |
| | 6,344,272 | B1 2/2002 Oldenburg et al. | 8,518,445 | B2 | 8/2013 | Alfano et al. |
| | 6,365,145 | B1 4/2002 Ben-Hur et al. | 8,591,924 | B2 | 11/2013 | Zheng |
| | 6,403,653 | B1 6/2002 Hobson et al. | 8,613,913 | B2 | 12/2013 | Chang et al. |
| | 6,410,603 | B1 6/2002 Hobson et al. | 8,617,580 | B2 | 12/2013 | Toledano et al. |
| | 6,428,811 | B1 8/2002 West et al. | 8,652,495 | B2 | 2/2014 | Porter et al. |
| | 6,461,595 | B1 10/2002 Leo et al. | 8,802,154 | B2 | 8/2014 | Harris et al. |
| | 6,491,929 | B1 12/2002 Anderson | 8,821,940 | B2 | 9/2014 | Harris et al. |
| | 6,517,820 | B1 2/2003 Robert | 8,821,941 | B2 | 9/2014 | Harris et al. |
| | 6,521,241 | B1 2/2003 Minerath, III et al. | 8,834,447 | B2 | 9/2014 | Chen et al. |
| | 6,530,944 | B2 3/2003 West et al. | 8,834,933 | B2 | 9/2014 | Harris et al. |
| | 6,534,044 | B1 3/2003 Wada et al. | 8,871,711 | B2 | 10/2014 | Cotsarelis et al. |
| | 6,541,017 | B1 4/2003 Lemann et al. | 8,895,071 | B1 | 11/2014 | Harris et al. |
| | 6,589,538 | B1 7/2003 Lemann et al. | 8,906,418 | B1 | 12/2014 | Harris et al. |
| | 6,600,951 | B1 7/2003 Anderson | 2001/0002275 | A1 | 5/2001 | Oldenburg et al. |
| | 6,620,407 | B1 9/2003 Gers-Barlag et al. | 2002/0009488 | A1 | 1/2002 | Francis et al. |
| | 6,645,517 | B2 11/2003 West et al. | 2002/0034480 | A1 | 3/2002 | Grimm et al. |
| | 6,660,381 | B2 12/2003 Halas et al. | 2002/0041854 | A1 | 4/2002 | Hadasch et al. |
| | | | 2002/0061363 | A1 | 5/2002 | Halas et al. |
| | | | 2002/0103517 | A1 | 8/2002 | West et al. |
| | | | 2002/0132045 | A1 | 9/2002 | Halas et al. |
| | | | 2002/0187172 | A1 | 12/2002 | Reb et al. |
| | | | 2002/0192298 | A1 | 12/2002 | Burrell et al. |
| | | | 2003/0060811 | A1 | 3/2003 | McDaniel |

(56)

References Cited

U.S. PATENT DOCUMENTS

| | | | | | | | |
|--------------|----|---------|--------------------------|--------------|-----|---------|---------------------------|
| 2003/0072728 | A1 | 4/2003 | Soane et al. | 2010/0204686 | A1 | 8/2010 | Yaroslavsky et al. |
| 2003/0095941 | A1 | 5/2003 | Anderson | 2010/0224026 | A1 | 9/2010 | Brennan Fournet et al. |
| 2003/0099718 | A1 | 5/2003 | Burrell et al. | 2010/0233222 | A1 | 9/2010 | Girier Dufournier et al. |
| 2003/0118657 | A1 | 6/2003 | West et al. | 2010/0254920 | A1 | 10/2010 | L'Alloret et al. |
| 2003/0156991 | A1 | 8/2003 | Halas et al. | 2010/0260700 | A1 | 10/2010 | Dop |
| 2003/0215638 | A1 | 11/2003 | Charnay et al. | 2010/0266647 | A1 | 10/2010 | Dingley et al. |
| 2004/0006328 | A1 | 1/2004 | Anderson | 2010/0266649 | A1 | 10/2010 | Maitra et al. |
| 2004/0151673 | A1 | 8/2004 | Josso | 2010/0272789 | A1 | 10/2010 | Satoh et al. |
| 2004/0166508 | A1 | 8/2004 | Pawlak et al. | 2010/0284924 | A1 | 11/2010 | Zink et al. |
| 2004/0170579 | A1 | 9/2004 | Mobius | 2010/0291166 | A1 | 11/2010 | Guyot-Ferreol et al. |
| 2004/0197286 | A1 | 10/2004 | Robert et al. | 2010/0291224 | A1 | 11/2010 | Tong et al. |
| 2004/0219179 | A1 | 11/2004 | McDaniel | 2010/0298758 | A1 | 11/2010 | Christansen et al. |
| 2004/0253138 | A1 | 12/2004 | Malak | 2010/0303716 | A1 | 12/2010 | Jin et al. |
| 2004/0253757 | A1 | 12/2004 | Gourlaouen et al. | 2010/0305495 | A1 | 12/2010 | Anderson et al. |
| 2005/0031655 | A1 | 2/2005 | Karpov | 2010/0323996 | A1 | 12/2010 | Ute et al. |
| 2005/0031658 | A1 | 2/2005 | Girier Dufournier et al. | 2011/0021970 | A1 | 1/2011 | Vo-Dinh et al. |
| 2005/0044642 | A1 | 3/2005 | Butcher | 2011/0034855 | A1 | 2/2011 | Esenaliev |
| 2005/0048546 | A1 | 3/2005 | Penn et al. | 2011/0052672 | A1 | 3/2011 | Krishnan et al. |
| 2005/0053629 | A1 | 3/2005 | Ueda et al. | 2011/0091572 | A1 | 4/2011 | Davidson |
| 2005/0058672 | A1 | 3/2005 | Gupta | 2011/0111002 | A1 | 5/2011 | Pop |
| 2005/0058678 | A1 | 3/2005 | Ricard et al. | 2011/0117202 | A1 | 5/2011 | Bourke, Jr. et al. |
| 2005/0059030 | A1 | 3/2005 | Bao et al. | 2011/0144030 | A1 | 6/2011 | Ramis Castellort et al. |
| 2005/0130324 | A1 | 6/2005 | West et al. | 2011/0159291 | A1 | 6/2011 | Sun et al. |
| 2005/0169866 | A1 | 8/2005 | Hannich et al. | 2011/0168200 | A1 | 7/2011 | Bourdin et al. |
| 2005/0175649 | A1 | 8/2005 | Disalvo et al. | 2011/0223255 | A1 | 9/2011 | Thiesen et al. |
| 2005/0186235 | A1 | 8/2005 | Martin et al. | 2011/0229559 | A1 | 9/2011 | Prestidge et al. |
| 2005/0187128 | A1 | 8/2005 | Martin et al. | 2011/0240556 | A1 | 10/2011 | Hoek et al. |
| 2005/0203495 | A1 | 9/2005 | Malak | 2011/0288234 | A1 | 11/2011 | Pandey |
| 2005/0220741 | A1 | 10/2005 | Dumousseaux | 2012/0021030 | A1 | 1/2012 | Matsufuji et al. |
| 2005/0229334 | A1 | 10/2005 | Huang et al. | 2012/0059307 | A1* | 3/2012 | Harris et al. 604/20 |
| 2006/0078578 | A1 | 4/2006 | Sandewicz et al. | 2012/0101007 | A1 | 4/2012 | Ahern et al. |
| 2006/0083762 | A1 | 4/2006 | Brun et al. | 2012/0141380 | A1 | 6/2012 | Margel et al. |
| 2006/0257336 | A1 | 11/2006 | Ferrari et al. | 2012/0289955 | A1 | 11/2012 | Marc |
| 2007/0032781 | A1 | 2/2007 | Henry et al. | 2013/0017238 | A1 | 1/2013 | Porter et al. |
| 2007/0065387 | A1 | 3/2007 | Beck et al. | 2013/0022655 | A1 | 1/2013 | Sachweh et al. |
| 2007/0092471 | A1 | 4/2007 | Cassier et al. | 2013/0023714 | A1 | 1/2013 | Johnston et al. |
| 2007/0104605 | A1 | 5/2007 | Hampden-Smith et al. | 2013/0183244 | A1 | 7/2013 | Hanes et al. |
| 2007/0125383 | A1 | 6/2007 | Ko | 2013/0195979 | A1 | 8/2013 | Tersigni |
| 2007/0154903 | A1 | 7/2007 | Marla et al. | 2013/0216596 | A1 | 8/2013 | Viladot Petit et al. |
| 2007/0158611 | A1 | 7/2007 | Oldenburg | 2013/0225901 | A1 | 8/2013 | Krishnan et al. |
| 2007/0160636 | A1 | 7/2007 | Kasai | 2013/0251825 | A1 | 9/2013 | Berry |
| 2007/0166248 | A1 | 7/2007 | L'Alloret et al. | 2013/0315650 | A1 | 11/2013 | Cassin et al. |
| 2007/0183992 | A1 | 8/2007 | Dumousseaux et al. | 2013/0315999 | A1 | 11/2013 | Paithankar et al. |
| 2007/0196305 | A1 | 8/2007 | Wang et al. | 2013/0323305 | A1 | 12/2013 | Paithankar et al. |
| 2007/0208400 | A1 | 9/2007 | Nadkarni et al. | 2013/0338545 | A1 | 12/2013 | Azhari et al. |
| 2007/0217996 | A1 | 9/2007 | Levy et al. | 2014/0005593 | A1 | 1/2014 | Harris et al. |
| 2007/0231940 | A1 | 10/2007 | Gourlaouen et al. | 2014/0012162 | A1 | 1/2014 | Harris et al. |
| 2008/0045865 | A1 | 2/2008 | Kislev | 2014/0012163 | A1 | 1/2014 | Harris et al. |
| 2008/0050448 | A1 | 2/2008 | Wilson et al. | 2014/0012183 | A1 | 1/2014 | Harris et al. |
| 2008/0204742 | A1 | 8/2008 | Halas et al. | 2014/0030300 | A1 | 1/2014 | Maitra et al. |
| 2008/0233060 | A1 | 9/2008 | Grune | 2014/0105982 | A1 | 4/2014 | Oldenburg et al. |
| 2008/0241262 | A1 | 10/2008 | Lee et al. | 2014/0120041 | A1 | 5/2014 | Prencipe et al. |
| 2008/0305337 | A1 | 12/2008 | Berning et al. | 2014/0120167 | A1 | 5/2014 | Lapotko et al. |
| 2009/0022765 | A1 | 1/2009 | Chung et al. | 2014/0120168 | A1 | 5/2014 | Oldenburg et al. |
| 2009/0022766 | A1 | 1/2009 | Geddes | 2014/0194900 | A1 | 7/2014 | Sedic |
| 2009/0053268 | A1 | 2/2009 | DePablo et al. | 2014/0205546 | A1 | 7/2014 | Macoviak |
| 2009/0123509 | A1 | 5/2009 | Berkland et al. | 2014/0243934 | A1 | 8/2014 | Vo-Dinh et al. |
| 2009/0175915 | A1 | 7/2009 | Maitra et al. | 2014/0271889 | A1 | 9/2014 | Messersmith et al. |
| 2009/0177122 | A1 | 7/2009 | Peterson | 2014/0303525 | A1 | 10/2014 | Sitharaman |
| 2009/0217465 | A1 | 9/2009 | Cremer et al. | 2014/0316387 | A1 | 10/2014 | Harris et al. |
| 2009/0226521 | A1 | 9/2009 | Smyth et al. | 2014/0316394 | A1 | 10/2014 | Quidant et al. |
| 2009/0246142 | A1 | 10/2009 | Bhatia et al. | 2014/0371654 | A1 | 12/2014 | Harris et al. |
| 2009/0291107 | A1 | 11/2009 | Schehlmann et al. | 2014/0371655 | A1 | 12/2014 | Harris et al. |
| 2009/0326614 | A1 | 12/2009 | El-Sayed et al. | 2014/0371656 | A1 | 12/2014 | Harris et al. |
| 2010/0002282 | A1 | 1/2010 | Agrawal et al. | 2014/0371658 | A1 | 12/2014 | Harris et al. |
| 2010/0016783 | A1 | 1/2010 | Bourke, Jr. | 2014/0371659 | A1 | 12/2014 | Harris et al. |
| 2010/0040549 | A1 | 2/2010 | Halas et al. | 2014/0371661 | A1 | 12/2014 | Harris et al. |
| 2010/0055138 | A1 | 3/2010 | Margulies | 2014/0371662 | A1 | 12/2014 | Harris et al. |
| 2010/0056485 | A1 | 3/2010 | Park | 2014/0371663 | A1 | 12/2014 | Harris et al. |
| 2010/0057068 | A1 | 3/2010 | Lee | 2014/0371664 | A1 | 12/2014 | Harris et al. |
| 2010/0104652 | A1 | 4/2010 | Biris et al. | 2015/0005691 | A1 | 1/2015 | Harris et al. |
| 2010/0119610 | A1 | 5/2010 | Schoen et al. | 2015/0045723 | A1 | 2/2015 | Paithankar et al. |
| 2010/0143431 | A1 | 6/2010 | Landau et al. | 2015/0165180 | A1 | 6/2015 | Anderson et al. |
| 2010/0172994 | A1 | 7/2010 | Sigmund et al. | 2015/0190341 | A1 | 7/2015 | Paithankar et al. |
| 2010/0174223 | A1 | 7/2010 | Sakamoto et al. | 2015/0196359 | A1 | 7/2015 | Paithankar et al. |
| | | | | 2015/0196452 | A1 | 7/2015 | Meyer et al. |

(56)

References Cited**U.S. PATENT DOCUMENTS**

2015/0196639 A1 7/2015 Lando et al.
 2015/0225599 A1 8/2015 Oldenburg et al.

FOREIGN PATENT DOCUMENTS

DE 10342258 4/2005
 DE 10351611 8/2005
 DE 102004002990 8/2005
 DE 102005007482 9/2006
 DE 102007020554 10/2008
 DE 102008052187 4/2010
 EP 409690 9/1993
 EP 518772 11/1994
 EP 518773 2/1995
 EP 555460 5/1995
 EP 614656 10/1996
 EP 586484 1/1998
 EP 0 601 130 B1 8/1998
 EP 0 712 322 B1 4/1999
 EP 0925807 A1 6/1999
 EP 0860123 B1 1/2002
 EP 966954 2/2002
 EP 1112325 5/2003
 EP 1185242 8/2005
 EP 1201219 12/2005
 EP 1325730 10/2006
 EP 1506764 4/2007
 EP 1506763 7/2007
 EP 1506765 7/2007
 EP 1506766 7/2007
 EP 1529513 3/2008
 EP 1317245 5/2008
 EP 1677843 8/2008
 EP 1744789 8/2008
 EP 1768749 10/2008
 EP 1267801 12/2008
 EP 1559393 5/2009
 EP 1559394 3/2010
 EP 1208005 4/2010
 EP 1861465 10/2010
 EP 1502574 11/2010
 EP 1167462 12/2010
 EP 2231283 9/2012
 EP 988853 10/2012
 EP 1263447 6/2013
 EP 2396010 8/2013
 EP 2416752 9/2013
 EP 1267747 1/2014
 EP 1959914 5/2014
 WO WO91/06894 5/1991
 WO WO 9533518 12/1995
 WO WO 96/20698 7/1996
 WO WO 9641579 12/1996
 WO WO 9700098 1/1997
 WO WO 99/46351 9/1999
 WO WO 00/02590 1/2000
 WO WO 0040266 7/2000
 WO WO 01/05586 1/2001
 WO WO 01/06257 1/2001
 WO WO 01/58458 8/2001
 WO WO 02/085385 10/2002
 WO WO 03/026481 4/2003
 WO WO 2004058352 7/2004
 WO WO 2004/086044 10/2004
 WO WO2005/077329 8/2005
 WO WO 2005/092286 10/2005
 WO WO 2006/122222 11/2006
 WO WO2008/079758 7/2008
 WO WO2008/079760 7/2008
 WO WO 2008/106966 9/2008
 WO WO 2009/117124 9/2009
 WO WO 2010/073260 7/2010
 WO WO2010/109545 9/2010
 WO WO 2010/116345 10/2010

WO WO 2010/116346 10/2010
 WO WO2010/137580 12/2010
 WO WO2011/013101 2/2011
 WO WO 2011/031871 3/2011
 WO WO 2011/116963 9/2011
 WO WO 2012/027728 3/2012
 WO WO2012/035029 3/2012
 WO WO2013/106998 7/2013
 WO WO2013/106999 7/2013
 WO WO2013/107000 7/2013
 WO WO2013/107001 7/2013
 WO WO2013/107002 7/2013
 WO WO2013/107349 7/2013
 WO WO2013/107350 7/2013
 WO WO2013/107351 7/2013
 WO WO2013/107352 7/2013
 WO WO2013/107353 7/2013
 WO WO2013/107354 7/2013
 WO WO 2013/158278 10/2013
 WO WO2013/160362 10/2013
 WO WO2013/169955 11/2013
 WO WO2014/026142 2/2014
 WO WO2014/052973 4/2014
 WO WO2014/145784 9/2014
 WO WO2014/145784 A1 9/2014

OTHER PUBLICATIONS

Divaris, et al. "Phototoxic Damage to Sebaceous Glands and Hair Follicles of Mice After Systemic Administration of 5-Aminolevulinic Acid Correlates with Localized Protoporphyrin IX Fluorescence", *American Journal of Pathology*, vol. 136, No. 4, Apr. 1990, pp. 891-897.
 Hongcharu, et al. "Topical ALA-Photodynamic Therapy for the Treatment of Acne Vulgaris", *Journal of Invest. Dermatology*, vol. 115, No. 2, Aug. 2000, pp. 1-10.
 Kjeldstad, et al. "Changes in Polyphosphate Composition and Localization in Propionibacterium Acnes After Near-Ultraviolet Irradiation", *Canadian Journal of Microbiology*, vol. 37, No. 7, Jul. 1991, 562-567 (Abstract, 1 Page).
 Koenig, et al. "Photodynamic-Induced Inactivation of Propionibacterium Acnes", *SPIE Proceedings, SPIE-Int. Soc. Opt. Eng.*, 106-110, vol. 3247, Jan. 1998 (Abstract, 3 Pages).
 Konig, et al. "Photodynamic Activity of Methylene Blue", *Aktuelle Dermatol.*, vol. 19, 1993, pp. 195-198.
 Konig, et al. "Photodynamically Induced Inactivation of Propionibacterium Acnes Using the Photosensitizer Methylene Blue and Red Light", *Dermatologische Monatsschrift (Dermatol Monatsschr)*, vol. 178, Apr. 1992, pp. 297-300.
 Lloyd, et al. "Selective Photothermolysis of the Sebaceous Glands for Acne Treatment", *Lasers in Surgery and Medicine*, vol. 31, 2002, pp. 115-120.
 Mills, et al. "Ultraviolet Phototherapy and Photochemotherapy of Acne Vulgaris", *Arch Dermatol.*, vol. 114, No. 2, Feb. 1978 (Abstract, 2 pages).
 Mutzhas, et al. "A New Apparatus with High Radiation Energy Between 320-460 nm: Physical Description and Dermatological Applications", *The Journal of Investigative Dermatology*, vol. 76, No. 1, Jan. 1981, pp. 42-47.
 Pento, et al. "Delta-Aminolevulinic Acid", *Drugs of the Future*, vol. 22, No. 1, 1997, pp. 11-17.
 Phillips, et al. "Medical Progress: Recent Advances in Dermatology", *New England Journal of Medicine*, vol. 326, No. 3, Jan. 1992, pp. 1-9 (167-176).
 Wainwright, Mark "Non-Porphyrin Photosensitizers in Biomedicine", *Chemical Society Reviews*, 1996, pp. 351-359.
 Amirthalingam et al. "Use of Silica-Gold Core Shell Structure Nanoparticles for Targeted Drug Delivery System" *J. Nanomedic Nanotechnol* 2:119, (2011) vol. 2, Issue 6.
 Bukasov et al. "Nano Letters—Highly tunable infrared extinction properties of gold nanocrescents." *American Chemical Society*, vol. 7, No. 5 May 2007, published on web Apr. 14, 2007.
 Ghaffarpour, Azizjalali M. et al., "CO₂ Laser therapy versus cryotherapy in treatment of genital warts; a Randomized Controlled Trial (RCT)", *Iranian Journal of Microbiology*, vol. 4, No. 4, Dec. 2012, 187-190.

(56)

References Cited

OTHER PUBLICATIONS

- Kulkarni et al., "Effect of Experimental Temperature on the Permeation of Model Diffusants Across Porcine Buccal Mucosa" AAPS PharmSciTech. Jun. 2011; 12(2)579.
- Lazare, M. What are Cold Sores (Herpetic Lesions)?, <http://www.drmarclazare.com/laser-treatments-for-cold-soresherpetic-lesions/>, dated Jul. 8, 2014.
- Lewicka et al. "Nanorings and nanocrescents formed via shaped nanosphere lithography: a route toward large areas of infrared metamaterials." *IOP Publishing, Nanotechnology* 24: Feb. 28, 2013.
- Maltzahn, Geoffrey von, et al., "Computationally Guided Photothermal Tumor Therapy Using Long-Circulating Gold Nanorod Antennas" *Cancer Res* 2009; 69: (9) Published online Apr. 14, 2009 as 10.1158/008-5472.CAN-08-4242.
- Rallis, Tena M., "Low-Intensity Laser Therapy for Recurrent Herpes Labialis" *The Journal of Investigative Dermatology*, vol. 115, No. 1 Jul. 2000.
- Prosecution history (excluding references of record) of U.S. Appl. No. 13/789,575, namely an Amendment and a Suggestion for Declaration of Interference (with Appendices) over US Publication 2014/0005593 with U.S. Appl. No. 14/020,481, now U.S. Pat. No. 8,821,941. The Amendment and Suggestion for Declaration of Interference (with Appendices) and related documentation is dated Jul. 28, 2015 (submission date to USPTO) (Part 1 of 5).
- Prosecution history (excluding references of record) of U.S. Appl. No. 13/789,575, namely Exhibits from a Suggestion for Declaration of Interference over US Publication 2014/0005593 with U.S. Appl. No. 14/020,481, now U.S. Pat. No. 8,821,941. The Exhibits from a Suggestion for Declaration of Interference and related documentation is dated Jul. 28, 2015 (submission date to USPTO) (Part 2 of 5).
- Prosecution history (excluding references of record) of U.S. Appl. No. 13/789,575, namely Exhibits from a Suggestion for Declaration of Interference over US Publication 2014/0005593 with U.S. Appl. No. 14/020,481, now U.S. Pat. No. 8,821,941. The Exhibits from a Suggestion for Declaration of Interference and related documentation is dated Jul. 28, 2015 (submission date to USPTO) (Part 3 of 5).
- Prosecution history (excluding references of record) of U.S. Appl. No. 13/789,575, namely Exhibits from a Suggestion for Declaration of Interference over US Publication 2014/0005593 with U.S. Appl. No. 14/020,481, now U.S. Pat. No. 8,821,941. The Exhibits from a Suggestion for Declaration of Interference and related documentation is dated Jul. 28, 2015 (submission date to USPTO) (Part 4 of 5).
- Prosecution history (excluding references of record) of U.S. Appl. No. 13/789,575, namely Exhibits from a Suggestion for Declaration of Interference over US Publication 2014/0005593 with U.S. Appl. No. 14/020,481, now U.S. Pat. No. 8,821,941. The Exhibits from a Suggestion for Declaration of Interference and related documentation is dated Aug. 19, 2015 (submission date to USPTO).
- Prosecution history (excluding references of record) of U.S. Appl. No. 13/789,575, namely an Advisory Action further to a Suggestion for Declaration of Interference over US Publication 2014/0005593 with U.S. Appl. No. 14/020,481, now U.S. Pat. No. 8,821,941. The Advisory Action and related documentation is dated Aug. 21, 2015 (mailing date from USPTO).
- Aherne, et al. "Optical Properties and Growth Aspects of Silver Nanoprisms Produced by Highly Reproducible and Rapid Synthesis at Room Temperature." *Advanced Materials, Adv. Funct. Mater.* Jul. 9, 2008, v18, 2005-2016.
- Ammad et al. "An assessment of the efficacy of blue light phototherapy in the treatment of acne vulgaris." *J. Cosmet Dermatol*, 2008, 7: 180-188.
- Charles et al. "Versatile Solution Phase Triangular Silver Nanoplates for Highly Sensitive Plasmon Resonance Sensing" *American Chemical Society NANO*, v4, No. 1 p. 55-64, Dec. 23, 2009.
- Chen et al. "Controlling 2-dimensional growth of silver nanoplates." *Self-Assembled Nanostructured Materials Symposium. Mat. Res. Soc. Symp. Proc.* vol. 775, 343-348ixiii+394. (2003).
- Chen et al. "Silver nanodisks: Synthesis, characterization, and self-assembly." *J. Phys. Chem. B*, vol. 106, No. 42, 2002 10777-10781. (Published Sep. 21, 2002).
- Chen, et al. "Silver nanoplates: Size control in two dimensions and formation mechanisms." *J. Phys. Chem. B* 2004, 108, 5500-5506 *Journal of Physical Chemistry B*, 108, 5500-5506. (Published Apr. 14, 2004).
- Chen, et al. "Synthesis and characterization of truncated triangular silver nanoplates." *Nano Letters*, 2002, 2 (9), 1003-1007. (Published Jul. 26, 2002).
- Choudhary and Elsaie, M.L. "Photodynamic therapy in dermatology: a review." *Lasers Med Sci.*, 2009, 24:971-980.
- Donnelly et al. "Photosensitizer delivery for photodynamic therapy. Part 1: Topical carrier platforms." *Expert Opin Drug Deliv.* 2008, 5:757-766.
- Gollnick et al. "Can we define acne as a chronic disease? If so, how and when?" *Am J Clin Dermatol*, 2008, 9:279-284.
- Grachtchouk et al. "Basal cell carcinomas in mice arise from hair follicle stem cells and multiple epithelial progenitor populations." *J Clin Invest*, 2011, 121: 1768-1781.
- Grams et al. "Permeant lipophilicity and vehicle composition influence accumulation of dyes in hair follicles of human skin," *Eur J Pharm Sci*, 2003, 18:329-336.
- Hao E. K., et al. "Synthesis of Silver Nanodisks using Polystyrene Mesospheres as Templates." *J Am Chem Soc*, 124, 15182-15183. (Published Nov. 22, 2002).
- Hao E., et al. "Synthesis and optical properties of anisotropic metal nanoparticles." *Journal of Fluorescence*, vol. 14, No. 4, Jul. 2004, 331-341. (Published Jul. 2004).
- He et al. "Surface Plasmon Resonances of Silver Triange Nanoplates: Graphic Assignments of Resonance Modes and Linear Fittings of Resonance Peaks" *J. Phys. Chem. B* 2005, 109, 17503-17511 (Published Aug. 20, 2005).
- He, et al. "The evidence for synthesis of truncated silver nanoplates in the presence of CTAB." *Materials Characterization*, 59, 380-384. (Published 2008).
- Hongcharu et al. "Topical ALA-photodynamic therapy for the treatment of acne vulgaris." *J Invest Dermatol*, 2000, 115:183-192.
- Huang et al. Microemulsification of triglyceride sebum and the role of interfacial structure on bicontinuous phase behavior.: *Langmuir*, 2004, 20:3559-3563.
- Jiang et al. "A self-seeding coreduction method for shape control of silver nanoplates" *Nanotechnology* 17 (2006) 4929-4935 (Published Sep. 11, 2006).
- Jin et al. "Photoinduced Conversion of Silver Nanospheres to Nanoprisms." *Science*, v 294, 1901-1903. (Published Nov. 30, 2001).
- Jin, et al. "Controlling anisotropic nanoparticle growth through plasmon excitation." *Nature*, v. 425, 487-490 (Published Oct. 2, 2003).
- Knorr et al. "Follicular transport route-research progress and future perspectives." *Eur J Pharm Biopharm*, 2009, 71:173-180.
- Lademann et al. "Nanoparticles—an efficient carrier for drug delivery into the hair follicles." *Eur J Pharm Biopharm*, 2007, 66:159-164.
- Le Guevel, et al. "Synthesis, Stabilization, and Functionalization of Silver Nanoplates for Biosensor Applications." *J Phys Chem C*, 113, 16380-16386. (Published Aug. 21, 2009).
- Mallon et al. "The quality of life in acne: a comparison with general medical conditions using generic questionnaires." *Br J Dermatol*, 1999, 140:672-676.
- Meidan, V.M. "Methods for quantifying intrafollicular drug delivery: a critical appraisal." *Expert Opin Drug Deliv*, 2010, 7:1095-1108.
- Metraux, G. S. M. et al "Rapid Thermal Synthesis of Silver Nanoprisms with Chemically Tailorable Thickness." *Advanced Materials*, 2005, 17, No. 4, 412-415. (Published Feb. 23, 2005).
- Mitragotri et al. "Synergistic effect of low-frequency ultrasound and sodium lauryl sulfate on transdermal transport." *J Pharm Sci*, 2000, 89:892-900.
- Mortensen et al. "In vivo skin penetration of quantum dot nanoparticles in the murine model: the effect of UVR." *Nano Lett*, 2008, 8:2779-2787.

(56)

References Cited**OTHER PUBLICATIONS**

- Nanni, C.A. and Alster, T.S. (1997). "Optimizing treatment parameters for hair removal using a topical carbon-based solution and 1064-nm Q-switched neodymium: YAG laser energy." *Arch Dermatol*, 1997, 133:1546-1549.
- Polat et al. "Ultrasound-mediated transdermal drug delivery: Mechanisms, scope, and emerging trends." *J Control Release*, 2011, 152:330-348.
- Rogers et al. "Hair removal using topical suspension-assisted Q-switched Nd: YAG and long-pulsed alexandrite lasers: A comparative study." *Dermatol Surg*, 1999, 25:844-844; discussion 848-850.
- Sakamoto et al. "Photodynamic therapy for acne vulgaris: A critical review from basics to clinical practice: Part I, Acne Vulgaris: When and why consider photodynamic therapy?" *Journal of the American Academy of Dermatology*, 2010, 63:183-193.
- Sakamoto et al. "Photodynamic therapy for acne vulgaris: a critical review from basics to clinical practice: Part II. Understanding parameters for acne treatment with photodynamic therapy." *Journal of the Academy of Dermatology*, 2010, 63:195-211.
- Schultz, et al. "The Chemorheology of Poly(vinyl alcohol)-Borate Gels." *Macromolecules*, vol. 2, No. 3, 281-285. (Published May-Jun. 1969).
- Sellheyer, K. "Basal cell carcinoma: cell of origin, cancer stem cell hypothesis and stem cell markers." *Br J Dermatol*, 2011, 164:696-711.
- Sellheyer, K. (2007). "Mechanisms of laser hair removal: could persistent photoepilation induce vitiligo or defects in wound repair?" *Dermatol Surg*, 2007, 33:1055-1065.
- Shershen et al. "Temperature-Sensitive Polymer—Nanoshell Composites for Photothermally Modulated Drug Delivery" *Journal of Biomedical Materials Research*; vol. 51, Issue 3, pp. 293-298 (Jun. 28, 2000).
- West et al. "Applications of Nanotechnology to Biotechnology" *Current Opinion in Biotechnology* 2000, 11:215-217; Published Apr. 1, 2000.
- Wong, S.Y., and Reiter, J.F. "Wounding mobilizes hair follicle stem cells to form tumors." *Proc Natl Acad Sci USA*, 2011, 108:4093-4098.
- Xiong, et al. "Synthesis of silver nanoplates at high yields by slowing down the polyol reduction of silver nitrate with polyacrylamide." *Journal of Materials Chemistry*, 17, 2600-2602. (Published May 17, 2007).
- Xue, et al. "pH-Switchable Silver Nanoprism Growth Pathways." *Angew. Chem. Int. Ed.*, 46, 2036-2038. (Published Feb. 13, 2007).
- Zhao, W., and Karp, J.M. "Tumour targeting: Nanoantennas heat up." *Nat Mater*, 2009, 8:453-454.
- Prosecution history (excluding references of record) of U.S. Appl. No. 13/789,575, including a 37 CFR 1.131 declaration over US Publication 2014/0005593 with U.S. Appl. No. 14/020,481, now U.S. Pat. No. 8,821,941. The 131 declaration is dated Dec. 31, 2014 (submission date to USPTO).

* cited by examiner

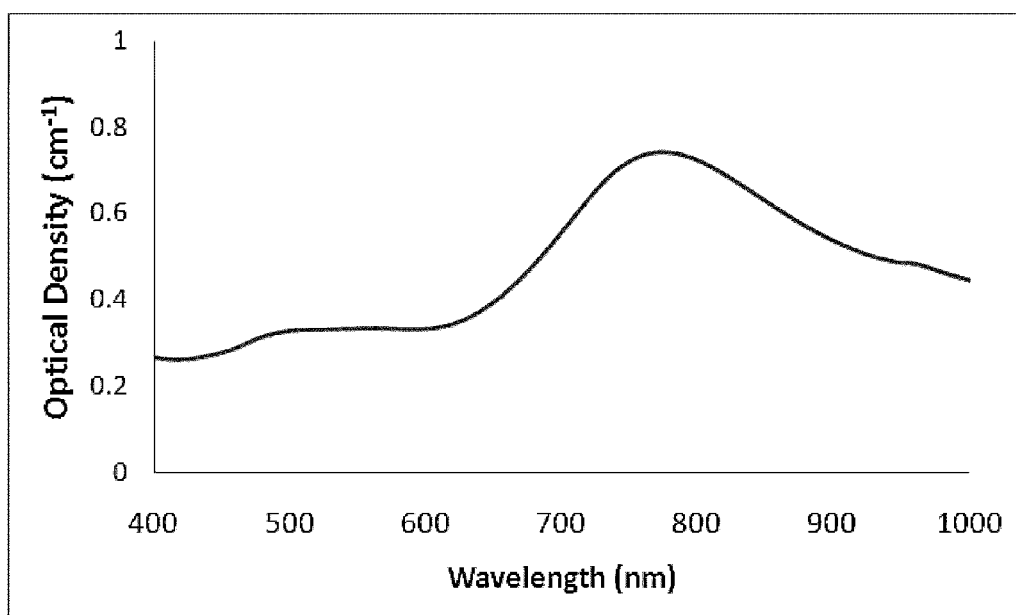


Figure 1

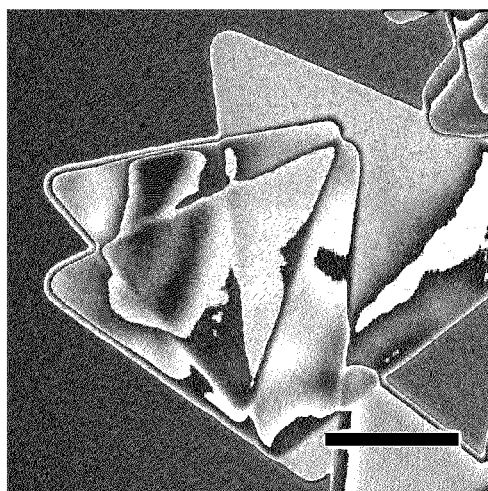


Figure 2

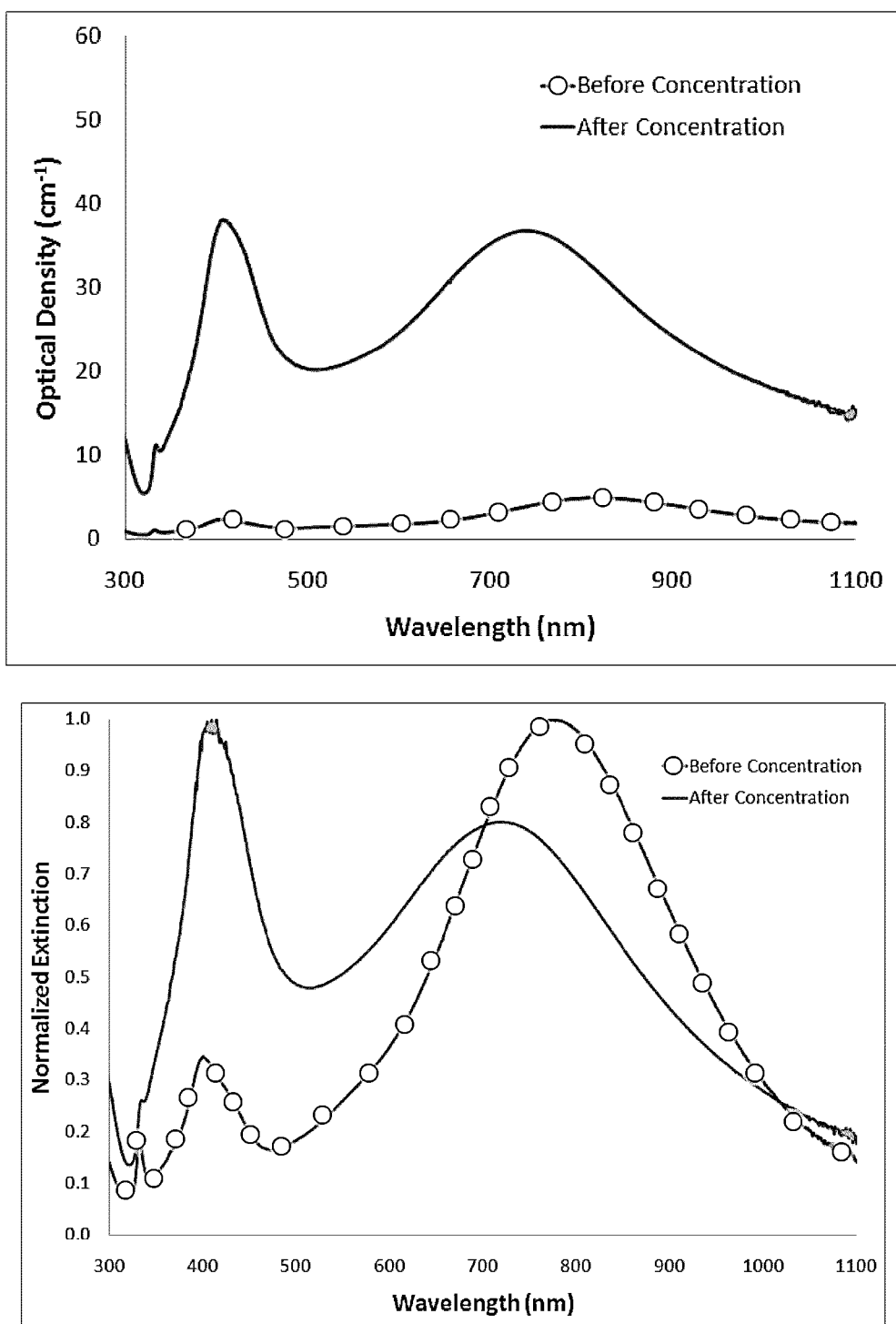


Figure 3

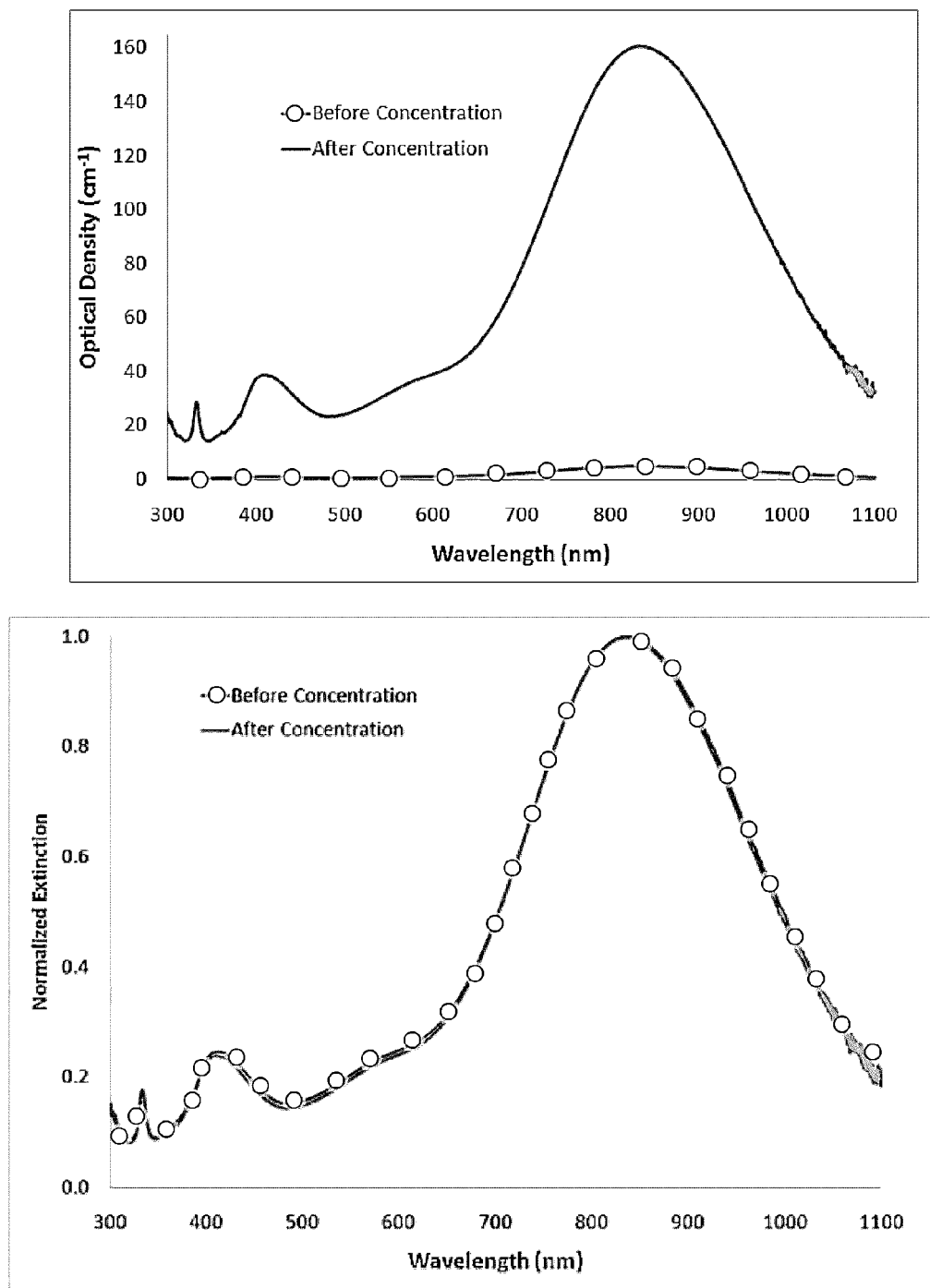


Figure 4

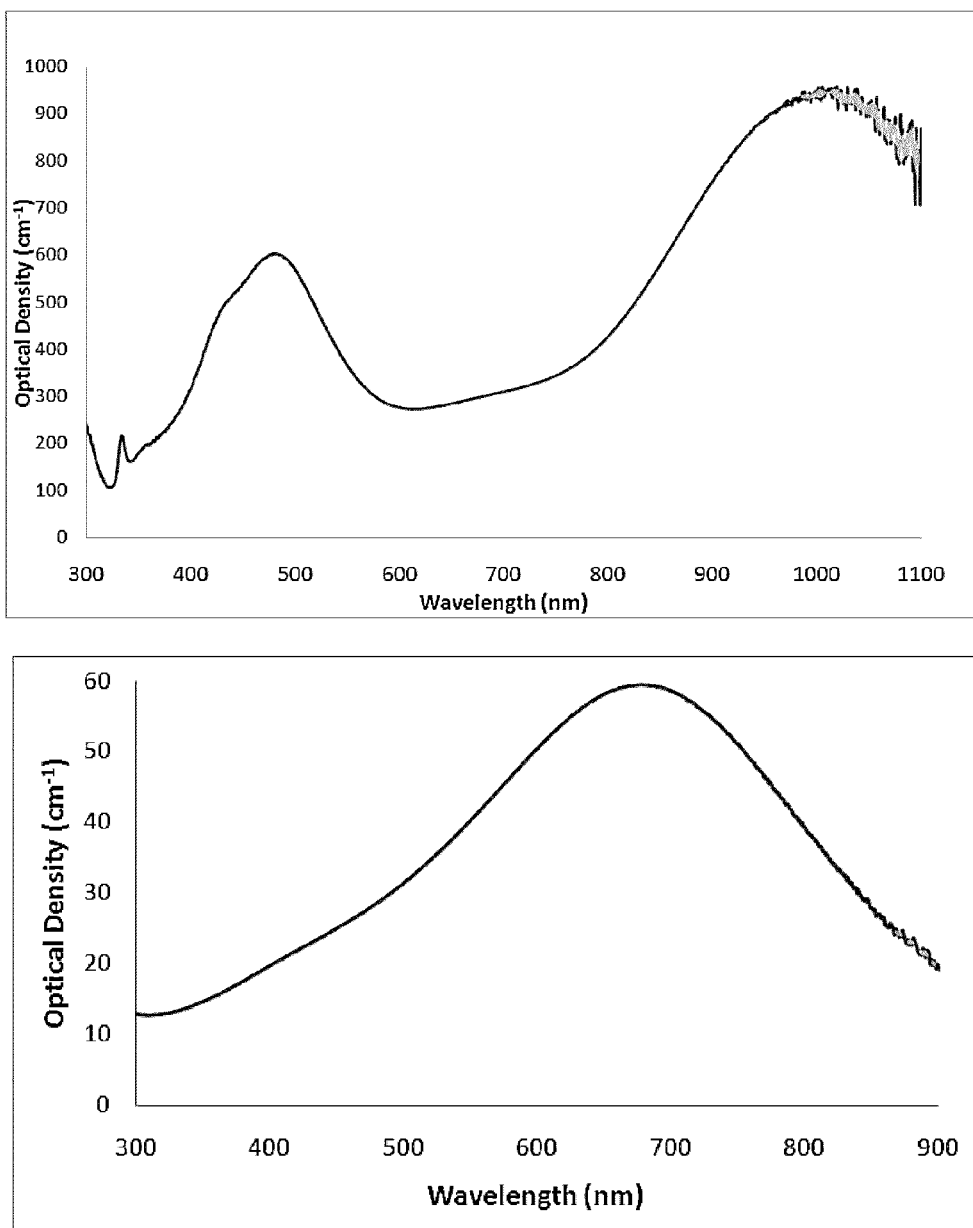


Figure 5

1

SILVER NANOPATE COMPOSITIONS AND METHODS

INCORPORATION BY REFERENCE TO ANY PRIORITY APPLICATIONS

This application claims the benefit of priority from U.S. Provisional Application 61/795,149, filed on Oct. 11, 2012, which is incorporated by reference in its entirety. Any and all applications for which a foreign or domestic priority claim is identified in the Application Data Sheet as filed with the present application are hereby incorporated by reference under 37 CFR 1.57.

PARTIES TO JOINT RESEARCH AGREEMENT

The invention described herein was created subject to a Joint Research Agreement between Sienna Labs, Inc. and nanoComposix, Inc.

BACKGROUND

1. Field of the Invention

Various embodiments of the invention relate to methods for preparing high optical density solutions of silver platelet nanoparticles (e.g., nanoplates) and to nanoparticles, solutions and substrates prepared by said methods.

2. Description of the Related Art

Nanoparticles, including nanospheres, nanorods, nanowires, nanocubes, nanoplates, as well as other shapes can be synthesized from a range of materials. Nanoparticles made from metals including gold and silver have unique optical properties which can be tuned to interact with light throughout the electromagnetic spectrum due to the localized surface plasmon resonance supported by these nanomaterials. Technologies that take advantage of the unique optical properties of silver nanoparticles, (e.g., such as silver nanoplates), include, but are not limited to, diagnostic, photonic, medical, and obscuring technologies. A subset of these technologies including photothermal tumor ablation, hair removal, acne treatment, wound healing, and antimicrobial applications among others, may use solutions of nanoparticles with high optical densities. Silver platelet nanoparticles, which are also known as silver nanoplates or silver nanoprisms, are of particular interest for technologies that utilize nanoparticle optical properties due to their tunable spectral peaks and extremely high optical efficiencies. While methods to fabricate silver platelet nanoparticles via photoconversion (Jin et al. 2001; Jin et al. 2003), pH-controlled photoconversion (Xue 2007), thermal growth (Hao et al. 2004; Hao 2002; He 2008; Metraux 2005), templated growth (Hao et al. 2004; Hao 2002), and seed mediated growth (Aherne 2008; Chen; Carroll 2003; Chen; Carroll 2002, 2004; Chen et al. 2002; He 2008; Le Guevel 2009; Xiong et al. 2007) have been developed, these methods generate relatively dilute solutions with correspondingly low visible and near-infrared optical densities, (e.g., such as optical densities of less than 10 cm^{-1} , such as $1\text{--}9\text{ cm}^{-1}$, $5\text{--}10\text{ cm}^{-1}$).

SUMMARY

For many silver nanoplate applications, a more concentrated solution of the silver nanoplates is of utility and can be particularly advantageous. In some instances, when the as-fabricated solutions of silver nanoplates are concentrated to yield a higher particle density under previously developed methods, the shape of the particle can undergo a change

2

resulting in a shift in the solution optical properties. In many cases, these changes result in an undesirable degradation of their optical properties. Accordingly, several embodiments of the present invention provide methods for preparing high optical density solutions of silver nanoplates from dilute silver nanoplate solutions that substantially or fully preserve the optical properties of as-fabricated silver nanoplates when the particle concentration is increased. The high optical density solutions of silver nanoplates can be exposed to substrates to generate nanoplate composites with high loading levels.

Various embodiments of the invention provide a method for preparing high optical density solutions of silver platelet nanoparticles, as well as the nanoparticles and solutions prepared by those methods. In one embodiment, the process comprises the replacement of one or more original components (e.g., chemical or biological agents) bound, or otherwise coupled to, the nanoparticle surface with a stabilizing agent. The stabilizing agent can be a biological or chemical agent that stabilizes the nanoplates before, during, and/or after concentration, thereby allowing for the production of a stable, high optical density solution of silver nanoplates. In one embodiment, the process also comprises a method of increasing the concentration of silver nanoplates within the solution, and thus increasing the solution optical density. In several embodiments, the stability (e.g., the characteristics of the nanoparticles in the solution, such as shape, size, optical properties, peak response, plasmonic properties, etc.) of the high optical density solution is unaffected or substantially unaffected during the process.

In one embodiment, a high optical density solution comprises silver nanoplates that have been stabilized with stabilizing agents (e.g., surface bound molecules chemical agents, and/or biological agents). In various embodiments, a solution of silver platelet nanoparticles (e.g., silver nanoplates) have been surface functionalized with chemical or biological agents that are physisorbed to the surface, molecularly bound to the surface through specific interactions, or encapsulate each nanoplate on its surface.

In one embodiment, a high optical density solution of silver nanoplates is associated with a substrate. In one embodiment, a portion of the nanoplates in solution bind to the substrate to create a nanoplate-substrate composite. The high optical density solutions of silver nanoplates can be exposed to substrates to generate nanoplate composites where a substantial portion of the surface area of a substrate is coated with nanoplates. In some embodiments the substrate comprises fibers, cloth, mesh, bandages, socks, wraps, other articles of clothing, sponges, high porosity substrates, particles with edge lengths greater than 1 micron, beads, hair, skin, paper, absorbent polymers, foam, wood, cork, slides, roughened surfaces, biocompatible substrates, filters, and/or medical implants.

In several embodiments, a process for increasing the optical density of a solution of stable, silver nanoplates comprises the following: (i) providing a solution comprising silver nanoplates having a plate shape, a first extinction spectra, and a first peak optical density between $0.1\text{--}10\text{ cm}^{-1}$; (ii) adding a concentration stabilizing chemical agent to the solution of silver nanoplates; and (iii) increasing the concentration of silver nanoplates using tangential flow filtration, thereby increasing the optical density of the solution to a second peak optical density greater than 10 cm^{-1} , wherein the silver nanoplates comprise the plate shape and the first extinction spectra at the optical density greater than 10 cm^{-1} .

In various embodiments, the stabilizing agent comprises or consists essentially of at least one of the group consisting of polyvinyl pyrrolidone, polyvinyl alcohol, polyethylene glycol, and dextran. In various embodiments, the stabilizing

agent comprises or consists essentially of at least one of the group consisting of polysulphonates, ethylene oxides, phenols, and carbohydrates. In one embodiment, the concentration stabilizing chemical agent is a water soluble polymer. In one embodiment, the concentration stabilizing chemical agent is a metal or metalloid oxide. In one embodiment, the stabilizing chemical agent is a silicon dioxide shell. In various embodiments, the silicon dioxide shell ranges in thickness from 1 nm to 100 nm. In one embodiment, the stabilizing chemical agent is a titanium dioxide shell. In various embodiments, a combination of stabilizing agents are used.

In various embodiments, the process further comprises adding any of the group selected from an acid, a base, and a buffering agent to the solution. In one embodiment, the silver nanoplates have an aspect ratio of between 1.5 and 25. In one embodiment, the nanoplate has an edge length between 10 nm and 250 nm. In some embodiments, the solution of silver nanoplates is formed using a seed mediated growth method. In one embodiment, the concentration of silver nanoplates is washed with between 1 and 5 wash volumes after increasing the concentration using tangential flow filtration. In one embodiment, the solution of silver nanoplates is incubated with a substrate.

In various embodiments, a process for generating a solution of silver nanoplates with high optical density comprises the following: (i) providing a solution of silver nanoplates with a first peak optical density between $0.1\text{--}10\text{ cm}^{-1}$, (ii) adding a concentration stabilizing chemical agent to the solution of silver nanoplates; (iii) adding a buffer to the solution of silver nanoplates; and (iv) increasing the concentration of the silver nanoplates to increase the optical density of the solution greater than 10 cm^{-1} .

In one embodiment, the concentration stabilizing chemical agent comprises a derivative of a vinyl polymer. In one embodiment, the polymer is polyvinyl alcohol (PVA). In one embodiment, the polymer is polyvinyl pyrrolidone (PVP). In one embodiment, the process further comprises adding one of the group consisting of sodium bicarbonate and sodium borate to the solution.

In several embodiments, a process for generating a solution of silver nanoplates with extremely high optical density comprises the following: (i) adding a concentration stabilizing chemical agent to a solution of silver nanoplates or precursor reagents and (ii) increasing the concentration of silver nanoplates to increase the optical density of the solution.

In various embodiments, the silver nanoplates have an aspect ratio of between 1.5 and 25 (e.g., 1.5-10, 25-50); and/or the nanoplate has an edge length between about 10 nm and 250 nm (e.g., 50-250, 65-100 nm); and/or the nanoplate is triangular in cross section; and/or the nanoplate is circular in cross section. In one embodiment, the perimeter of the nanoplate cross section has between 4 and 8 edges (e.g., 4, 5, 6, 7, 8). In various embodiments, the solution of silver nanoplates is formed using one or more of a photoconversion method, a pH-controlled photoconversion method, a thermal growth method, a seed mediated growth method, and/or a solution comprising a shape stabilizing agent or agents and a silver source. In various embodiments, chemical or biological agents, and/or electromagnetic radiation, and/or heat, or a combination thereof are used to reduce the silver source. In one embodiment, the solution of silver nanoplates is formed from some combination of a reducing agent, a shape stabilizing agent, a light source, a heat source, and a silver source.

In one embodiment, an acid, base, or buffering agent is added to change the solution pH. In various embodiments, the concentration stabilizing chemical agent is added prior to, during, and/or after the formation of the silver nanoplates. In

one embodiment, the concentration stabilizing chemical agent acts as a shape stabilizing agent. In one embodiment, the concentration stabilizing chemical agent acts as a reducing agent. In one embodiment, the concentration stabilizing chemical agent acts as an agent to change the solution pH.

In one embodiment, the concentration stabilizing chemical agent is a water soluble polymer. In various embodiments, the polymer is any one or more of a derivative of polysulfonate, sodium polystyrene sulfonate, a derivative of a vinyl polymer, and a polyvinyl alcohol (PVA). In various embodiments, the PVA has a molecular weight of less than about 80,000 Dalton (e.g., 1,000-50,000, 25,000-75,000 Dalton), between about 80,000 Dalton and 120,000 Dalton (e.g., 85,000-95,000, 100,000-110,000 Dalton), and/or more than about 120,000 Dalton (e.g., 150,000-300,000 Dalton). In one embodiment, the polymer is polyvinylpyrrolidone (PVP). In various embodiments, the PVP has a molecular weight of less than about 20,000 Dalton (e.g., 2,000-12,000 Dalton), more than about 20,000 Dalton (e.g., 35,000-400,000 Dalton), between about 20,000 Dalton and 60,000 Dalton (e.g., 40,000-55,000 Dalton), and/or more than about 60,000 Dalton (e.g., 70-100,000, 90-150,000 Dalton). In one embodiment, the polymer is an ethylene oxide derivative.

In one embodiment, the polymer is a polyethylene glycol (PEG). In various embodiments, the PEG has a molecular weight of less than about 5,000 Dalton (e.g., 200-3,000, 1,000-4,500 Dalton), between about 5,000 Dalton and 10,000 Dalton (e.g., 7,000-8,000, 6,000-7,500 Dalton), and/or more than about 10,000 Dalton (e.g., 12,000-35,000, 18,000-45,000 Dalton). In one embodiment, the PEG contains a single functional group. In one embodiment, the PEG contains more than one functional group (e.g., two, three, or more functional groups). In one embodiment, the functional group or groups comprise any of an amine, thiol, acrylate, alkyne, maleimide, silane, azide, hydroxyl, lipid, disulfide, fluorescent molecule, and/or biotin. In one embodiment, the functional group or groups can be any one or more of an amine, thiol, acrylate, alkyne, maleimide, silane, azide, hydroxyl, lipid, disulfide, fluorescent molecule, and/or biotin. In one embodiment, the concentration stabilizing agent is a carbohydrate derivative. In various embodiments, the polymer is a monosaccharide, a disaccharide, an oligosaccharide, a polysaccharide, and/or dextran. In various embodiments, the dextran has a molecular weight that is less than about 2,000 Dalton (e.g., 200-1,400, 1,000-1,900 Dalton), between about 2,000 Dalton and 5,000 Dalton (e.g., 3,000-3,500, 2,000-4,000 Dalton), and/or more than about 5,000 Dalton (e.g., 6,000-8,000, 7,000-13,000 Dalton).

In various embodiments, the concentration stabilizing chemical agent is any one or more of a phenol, a monomeric phenol, a dimeric phenol, a trimeric phenol, a polyphenol, a tannic acid, is gum Arabic, a biological molecule, a protein, a bovine serum albumin, streptavidin, biotin, a peptide, an oligonucleotide, a naturally occurring oligonucleotide, a synthetic oligonucleotide, a metal or metalloid oxide, and/or a silicon dioxide shell. In one embodiment, a silicon dioxide shell has ranges in thickness from about less than 1 nm to about 100 nm (e.g., 10-70, 30-90, 40-60 nm). In one embodiment, a combination of stabilizing agents are used. In various embodiments, the solvent can be one or more of water, an alcohol, ethanol, isopropyl alcohol, t-butanol, a mixture of a water and an alcohol.

In one embodiment, the concentration of silver nanoplates is increased using tangential flow filtration. In one embodiment, the tangential flow filtration is performed using a tangential flow filter membrane. In one embodiment, the tangential flow membrane is made from a cellulose ester or mix of

5

cellulose esters. In various embodiments, the tangential flow membrane is made from one or more of polyethersulfone and/or polysulfone. In various embodiments, the tangential flow membrane has a molecular weight cut off of less than about 10 kD (e.g., 1-5, 8 kD), of between about 10 kD and 500 kD (e.g., 50-250, 300-400 kD), of more than about 500 kD (e.g., 750, 1000, 5000 kD or more), of less than about 0.05 μm , of between about 0.05 μm and 0.5 μm (e.g., 0.01, 0.03 μm), and/or of more than about 0.5 μm (e.g., 1.0, 2, 5, 10, 100 μm).

In various embodiments, the silver nanoplate solution is concentrated to produce a solution with an optical density of greater than about 10 cm^{-1} (e.g., $15\text{--}45\text{ cm}^{-1}$, $30\text{--}150\text{ cm}^{-1}$, or more), greater than about 50 cm^{-1} (e.g., $80\text{--}150\text{ cm}^{-1}$, $60\text{--}120\text{ cm}^{-1}$, 100 cm^{-1} or more), greater than about 75 cm^{-1} (e.g., $80\text{--}110\text{ cm}^{-1}$, $200\text{--}400\text{ cm}^{-1}$, 1000 cm^{-1} or more), greater than about 100 cm^{-1} (e.g., $150\text{--}350\text{ cm}^{-1}$, $200\text{--}400\text{ cm}^{-1}$ or more), and/or greater than about 500 cm^{-1} (e.g., $600\text{--}1500\text{ cm}^{-1}$, 1000 cm^{-1} or more).

In one embodiment, the solvent of the concentrated solution is exchanged using tangential flow filtration. In one embodiment, the concentrated solution is processed to remove residual chemicals using tangential flow filtration.

In various embodiments, a solution of nanoparticles comprising silver nanoparticles is coated with a polymer with an optical density greater than 100 cm^{-1} (e.g., $160\text{--}550\text{ cm}^{-1}$, $900\text{--}1100\text{ cm}^{-1}$, 100 cm^{-1} , 1000 cm^{-1} or more).

In one embodiment, the solution of silver nanoplates is incubated with a substrate (e.g., fibers, cloth, mesh, bandages, socks, wraps, other articles of clothing, sponges, high porosity substrates, particles with edge lengths greater than 1 micron, beads, hair, skin, paper, absorbent polymers, foam, wood, cork, slides, roughened surfaces, biocompatible substrates, filters, and/or medical implants). In one embodiment, the substrate is removed from the solution of silver nanoplates and dried.

BRIEF DESCRIPTION OF THE DRAWINGS

Further objects, features and advantages of the invention will become apparent from the following detailed description taken in conjunction with the accompanying figures showing illustrative embodiments of the invention, in which the following is a description of the drawings. The drawings are examples, and should not be used to limit the embodiments. Moreover, recitation of embodiments having stated features is not intended to exclude other embodiments having additional features or other embodiments incorporating different combinations of the stated features. Further, features in one embodiment (such as in one figure) may be combined with descriptions (and figures) of other embodiments.

FIG. 1 illustrates the optical spectrum of a silver nanoplate solution as fabricated using a photoconversion method according to one embodiment of the present invention. In one embodiment, a silver nanoplate solution is fabricated using a photoconversion method identified as [DSS1099, alternative spectrum ARS1134]—as fabricated, these silver nanoplates have an optical density of less than 1 cm^{-1} .

FIG. 2 illustrates a transmission electron micrograph of silver nanoplates fabricated using a photoconversion method according to one embodiment of the present invention. Scale bar is 50 nm.

FIG. 3 illustrates one embodiment of plates concentrated in the absence of a concentration stabilizing agent with normalized (bottom) and unnormalized (top) extinction spectra of as-fabricated silver nanoplates before and after tangential flow filtration concentration. After concentration the plates

6

have a significantly changed peak shape as demonstrated by the normalized plot, and a spectral peak at 400 nm that demonstrates that a large number of silver nanoplates have turned into silver nanospheres. In one embodiment, plates are concentrated with the identification [MGM1201 and 1195E].

FIG. 4 illustrates one embodiment of plates concentrated in the presence of a concentration stabilizing agent with normalized (bottom) and unnormalized (top) extinction spectra of as-fabricated silver nanoplates before and after tangential flow filtration concentration using a concentration stabilizing agent. After being concentrated the plates retain their spectral peak shape with no increase in the spectral peak at 400 nm. In one embodiment, plates are concentrated with the identification [MGM1282 and 1279A].

FIG. 5 illustrates extinction spectra of high optical density nanoplate solutions processed using the methods described in various embodiments of the invention.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

Several embodiments of the present invention comprise processes for making solutions of plasmonic nanoparticle including silver nanoplates that are suitable for performing treatment of a target body region (e.g., such as for tumor ablation, hair removal, acne treatment, wound healing, and antimicrobial applications). Optical Density (O.D.) is the logarithmic ratio of the radiation incident on a material to the radiation transmitted through the material ($\text{O.D.} = -\log_{10}(I_t/I_0)$) where I_t is the intensity of transmitted light and I_0 is the intensity of the incident light). For solutions, the optical density is a function of the path length through the liquid sample is expressed in units of cm^{-1} . In some instances, optical density is expressed without the unit cm^{-1} —such as in instances in which a standard path length of 1 cm is used.

Silver Nanoplate Physical Description

In one embodiment, silver nanoplates are characterized by lengths along the three principle axes wherein: the axial length of two of the principle axes is at least two times greater than the axial length of the shortest principle axis and the shortest principal axial length is less than about 500 nm.

The ratio of the average of the two longer principle axes to the shorter principle axes is referred to as the aspect ratio. In one embodiment the average aspect ratio of the silver plates is greater than 1.5, 2, 3, 4, 5, 7, 10, 20, 30, or 50, or any range therein (e.g., greater than 8, 9, 11, 12, 13, 14, 15, 25, 35, 40, 45). In various embodiments the average aspect ratio of the silver plates is between 1.5 and 25, 2 and 25, 1.5 and 50, 2 and 50, 3 and 25, or 3 and 50 (e.g., 5 and 20, 10 and 15, 5 and 40, 5 and 30, 5 and 20, 10 and 50, 20 and 50, 30 and 50, 40 and 50, 10 and 20, 20 and 30, 30 and 40, 40 and 50, and any values between 1.5 and 50, inclusive).

In one embodiment the nanoplate has edge lengths less than 500 nm, 250 nm, 200 nm, 150 nm, 100 nm, 80 nm, 60 nm or 50 nm (e.g., 400 nm, 300 nm, 225 nm, 175 nm, 125 nm, 90 nm, 70 nm, 55 nm, and any values between 500 and 50 nm, inclusive). In one embodiment the nanoplate has edge lengths greater than 5 nm, 10 nm, 20 nm, 30 nm, 50 nm or 100 nm, or any value therein or more (e.g., 15, 25, 40, 60, 70, 75, 80, 90, 5-100, 20-80, 30-50, 45-95 nm, and/or 30 nm to 100 nm, 20 nm to 150 nm, 10 nm to 200 nm, 10 nm to 300 nm). In one embodiment the nanoplate has a thickness (third principle axis) that is less than 500 nm, 300 nm, 200 nm, 100 nm, 80 nm, 60 nm, 50 nm, 40 nm, 30 nm, 20 nm, or 10 nm, or any value therein (e.g., 400 nm, 250 nm, 150 nm, 75 nm, 5 nm to 20 nm, 5 nm to 30 nm, 10 nm to 30 nm, 10 nm to 50 nm, 10 nm to 100 nm).

Silver nanoplates have a variety of different cross sectional shapes including circular, triangular, or shapes that have any number of discrete edges. In one embodiment the nanoplates have less than 20, 15, 10, 8, 6, 5, or 4 edges (e.g., 18, 12, 11, 9, 2, 1). In one embodiment the nanoplates have more than 2, 3, 4, or 5 edges (e.g., 6, 7, 10, 15, 20 or more). In some embodiments the silver nanoplates have sharp corners and in other embodiments the corners are rounded. In some embodiments of silver nanoplates, there are a variety of different cross sectional shapes within the same sample. In other embodiments of silver nanoplate solutions greater than 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, or 90% of the number of particles in solution are silver nanoplates with the other particles having different shapes including but not limited to spherical, cubic, and irregular. In one embodiment the nanoplates have one or two flat sides. In another embodiment the nanoplates are pyramidal.

Silver Nanoplate Fabrication

The silver nanoplates utilized in various embodiments of this invention may be fabricated using photoconversion (Jin et al. 2001; Jin et al. 2003), pH controlled photoconversion (Xue 2007), thermal growth (Hao et al. 2004; Hao 2002; He 2008; Metraux 2005), templated growth (Hao et al. 2004; Hao 2002), seed mediated growth (Aherne 2008; Chen; Carroll 2003; Chen; Carroll 2002, 2004; Chen et al. 2002; He 2008; Le Guevel 2009; Xiong et al. 2007), or alternative methods. Alternative methods include methods in which the silver nanoplates are formed from a solution comprising a shape stabilizing agent or agents and a silver source, and in which chemical agents, biological agents, electromagnetic radiation, or heat are used to reduce the silver source.

FIG. 1 illustrates the optical spectrum of a silver nanoplate solution as fabricated using a photoconversion method according to one embodiment of the present invention. In one embodiment, a silver nanoplate solution is fabricated using a photoconversion method identified as [DSS1099, alternative spectrum ARS1134]—as fabricated, these silver nanoplates have an optical density of less than 1 cm^{-1} .

FIG. 2 illustrates a transmission electron micrograph of silver nanoplates fabricated using a photoconversion method according to one embodiment of the present invention. In FIG. 2, the scale bar is 50 nm.

FIG. 3 illustrates one embodiment of plates concentrated in the absence of a concentration stabilizing agent with normalized (bottom) and unnormalized (top) optical extinction spectra of as-fabricated silver nanoplates before and after tangential flow filtration concentration. After concentration the plates have a significantly changed peak shape as demonstrated by the normalized plot, and a spectral peak at 400 nm that demonstrates that a large number of silver nanoplates have turned into silver nanospheres. In one embodiment, plates are concentrated with the identification [MGM1201 and 1195E].

FIG. 4 illustrates one embodiment of plates concentrated in the presence of a concentration stabilizing agent with normalized (bottom) and unnormalized (top) optical extinction spectra of as-fabricated silver nanoplates before and after tangential flow filtration concentration using a concentration stabilizing agent. After being concentrated the plates retain their spectral peak shape with no increase in the spectral peak at 400 nm. In one embodiment, plates are concentrated with the identification [MGM1282 and 1279A].

FIG. 5 illustrates optical extinction spectra of high optical density nanoplate solutions processed using the methods described in various embodiments of the invention.

Silver Nanoplate Coating

In one embodiment, silver nanoplates have molecules that are adsorbed or otherwise bound to the particle surface. The molecules on the surface are the reactants or reactant by-products of the synthesis. One object of one embodiment of this invention is to partially or fully exchange the molecules that are bound to the surface of the silver nanoplates with other molecules that more fully protect the particles from changing shape during concentration. Another object of one embodiment of the invention is to use a stabilizing agent during fabrication that generates plate shapes and also stabilizes the nanoplates during subsequent concentration.

In various embodiments, stabilizing agent variants that may be utilized include chemical or biological agents that are physisorbed to the surface, molecularly bound to the surface through specific interactions (e.g. thiol or amine), or encapsulate the surface (i.e. a metal oxide or metalloid oxide shell). In various embodiments, specific chemical agents of interest include polymers such as polysulphonates, vinyl polymers, carbohydrates, ethylene oxides, phenols, and carbohydrates. In various embodiments, specific examples of these polymers include poly(sodium) styrene sulfonate, polyvinyl alcohol, polyvinyl pyrrolidone, tannic acid, dextran, and polyethylene glycol (PEG) including PEG molecules which contain one or more chemical groups (e.g. amine, thiol, acrylate, alkyne, maleimide, silane, azide, hydroxyl, lipid, disulfide, fluorescent molecule, or biomolecule moieties). In various embodiments, specific biomolecules of interest include proteins, peptides, and oligonucleotides, including biotin, bovine serum albumin, streptavidin, neutravidin, wheat germ agglutinin, naturally occurring and synthetic oligonucleotides and peptides, including synthetic oligonucleotides which have one or more chemical functionalities (e.g. amine, thiol, dithiol, acrylic phosphoramidite, azide, digoxigenin, alkynes, or biomolecule moieties). Specific encapsulating chemical agents of interest include metal oxide shells such as SiO_2 and TiO_2 . Stabilizing agents may be added prior to the formation of silver nanoplates, during the formation of silver nanoplates, or after the formation of silver nanoplates. An additional chemical agent of interest is gum arabic.

Carrier Solutions

In one embodiment of this invention the silver nanoplates are fabricated in aqueous solutions. In other embodiments the silver nanoplates are fabricated in other solutions that can include ethanol, isopropanol, or organic solvents such as heptane, toluene, or butanol.

In one embodiment an acid, base or buffering agent (e.g., a buffer) is added to change the solution pH either before, during, or after the addition of a stabilant. In various embodiments, the nanoplates are suspended in a sodium bicarbonate buffer or a sodium borate buffer.

Surface Stabilization

In various embodiments, stabilizing agents can be solid or liquid formulations that are added to the silver plate solution. The stabilizing agents have an affinity for the surface of the silver nanoplates and will associate with the plate surface. In some embodiments, the bound molecules on the silver nanoplates will be displaced by the added stabilizing agents. In some embodiments the stabilants are added to the as-fabricated silver nanoplate solution. In other embodiments, the solution of nanoplates is washed, or the residual reactants are otherwise removed. In other embodiments, the suspending solution is exchanged with a different suspending media which includes ethanol, isopropanol, or other polar or non-polar liquids before the stabilizing agents are added.

Once the stabilizing agent is added, the mixture of the stabilant and the silver nanoplates can undergo a number of

different processes including heating, boiling, boiling under reflux, rotoevaporation, vacuum, stirring, stirring with magnetic stir bars, stirring with overhead mixers, stirring with homogenizers, shaking, microfluidization, refrigeration, and freezing.

Washing and Concentrating

In one embodiment, after the stabilization step is complete, the silver nanoplates can be washed to remove residual reactants or to exchange the solution with another solution. In various embodiments, the exchange of solution can be accomplished using dialysis, centrifugation, filtration, or tangential flow filtration. One embodiment of the invention is where the number of wash volumes exchanged within the sample is 1, 2, 3, 4, 5, between 1 and 5, between 5 to 10, between 10 to 20, or more than 20 wash volumes.

High optical density solutions of the nanoparticles can be fabricated using centrifugation, evaporation, filtration, dialysis or tangential flow filtration. One embodiment of this invention utilizes tangential flow filtration as the process of concentrating the silver nanoplate solution. The filter membrane utilized may be formed from a variety of materials. Specific filter membrane materials of interest include cellulose esters, polysulfone, and polyethersulfone. The filter membrane utilized may have pores with a molecular weight cutoff of less than about 10 kD, between 10 kD to 500 kD, or more than about 500 kD (e.g., between 10 kD, to 100 kD, 10 kD to 500 kD, 20 kD to 500 kD, 20 kD to 250 kD), and/or pore sizes of less than about 0.05 μm between 0.05 μm and 0.5 or larger than about 0.5 μm (e.g., between 0.02 μm and 0.1 μm , 0.05 μm and 0.2 μm , 0.05 μm and 0.5 μm , 0.10 μm and 0.2 μm , 0.1 μm and 0.5 μm). Tangential flow filtration can also be utilized to change the solvent in which the silver nanoplates are dispersed. Specific solvents of interest include water and alcohols (e.g. t-butanol, ethanol, and isopropyl alcohol), as well as other polar or non-polar solvents. Additionally, tangential flow filtration can be utilized to remove residual chemicals.

This invention includes embodiments in which the silver nanoplate solution concentration is increased to produce a final solution with optical densities of greater than about 5 cm^{-1} , greater than about 10 cm^{-1} , greater than about 50 cm^{-1} , greater than about 75 cm^{-1} , greater than about 100 cm^{-1} , greater than about 500 cm^{-1} , or greater than about 1000 cm^{-1} (e.g., between 10 cm^{-1} to 100 cm^{-1} , 30 cm^{-1} to 300 cm^{-1} , 50 cm^{-1} to 500 cm^{-1} , 100 cm^{-1} to 1000 cm^{-1} , 300 cm^{-1} to 3000 cm^{-1} , or 500 cm^{-1} to 5000 cm^{-1}). One embodiment of the invention is where the silver nanoplate solution concentration is increased to above 10^6 , 10^7 , 10^8 , 10^9 , 10^{10} , 10^{11} , 10^{12} , 10^{13} particles per milliliter.

Storage

One embodiment of the invention is where the concentrated particles are stored at temperatures below -10 , 0 , 4 , 6 , 10 , or 20 degrees C.

One embodiment of the invention is where the particles are frozen and dried under vacuum. One embodiment is where the particles are freeze dried. One embodiment is where the particles are supercritically dried. Another embodiment is where an additional stabilant or other cryoprotectant is added to the solution before the particles are heat dried or freeze dried.

Composites

In one embodiment of the invention, high optical density solutions of silver nanoplates are associated with a substrate. Examples of substrates include fibers, cloth, mesh, bandages, socks, wraps, other articles of clothing, sponges, high porosity substrates, particles with diameters greater than 1 micron, beads, hair, skin, paper, absorbent polymers, foam, wood, cork, slides, roughened surfaces, biocompatible substrates,

filters, or medical implants. In one embodiment, the high optical density solutions of silver nanoplates at a concentration of at least 1 mg/mL, 10 mg/mL, 100 mg/mL (e.g., 1 to 10, 3 to 30, 5 to 50, 10 to 20, 5 to 50, 3 to 50, 1 to 100 mg/mL, 10 to 100, 20 to 100, 30 to 100 mg/mL) are incubated with the substrate. In another embodiment, the high optical density solutions of silver nanoplates at a concentration of at least 1 mg/mL, 10 mg/mL, or 100 mg/mL (e.g., 1 to 10, 3 to 30, 5 to 50, 10 to 20, 5 to 50, 3 to 50, 1 to 100 mg/mL, 10 to 100, 20 to 100, 30 to 100 mg/mL) are incubated with the substrate. In another embodiment the silver nanoplates are prepared at an optical density of at least 10, 100, 300, 500, 1000, or 2000 cm^{-1} (e.g., between 10-100, 20-200, 30-300, 50-500, 100-1000, 200-1000, 300-1000, 500-1000, or 200-2000 cm^{-1}) before incubating with the substrate. In another embodiment the substrate is chemically treated to increase the binding of the nanoplates to the substrate. For example, the substrate could be functionalized with a molecule that yielded a positively or negatively charged surface. In another embodiment, the pH of the incubating solution is selected in order to optimize binding. In another embodiment, the silver nanoplates cover at least 5%, 10%, 20%, 30%, 50% or 75% of the substrate (e.g., 5% to 10%, 10% to 100%, 10% to 50%, 50% to 100%, 30% to 100%, 30% to 70%, 40% to 80%, 50% to 90%, 60% to 100%, 70% to 100%, 80% to 100%, 90% to 100%, 0% to 5%, 1% to 10%, 2% to 20%, 5% to 30%, and/or 1% to 50% of the substrate). In another embodiment, other solvents or chemicals are added to the incubation solution. In another embodiment a biological linker (e.g. antibodies, peptides, DNA) is used to bind the high optical density silver nanoplates to the surface of the substrate. In one embodiment, the incubation is for less than 1 minute, 5 minutes, 20 minutes, 60 minutes, or 120 minutes (e.g., 0 to 1 minute, 1 minute to 120 minutes, 5 minutes to 120 minutes, 20 minutes to 120 minutes, 60 minutes to 120 minutes, 5 minutes to 60 minutes, 10 minutes to 60 minutes, 20 minutes to 60 minutes, 0 minutes to 10 minutes, 0 minutes to 20 minutes, or 0 minutes to 5 minutes).

In one embodiment, the substrate is separated from the incubating solution and dried. The substrate can be dried using air drying, heat drying, freeze drying, or supercritical drying. In another embodiment the dried substrate can be further processed by soaking the substrate in another material, painting the substrate with another material, or exposing the substrate to another material that is in the vapor phase.

Other embodiments of the invention will be apparent to those skilled in the art from consideration of the specification and practice of the invention disclosed herein. It is intended that the specification and examples be considered as disclosing certain embodiments of the invention only, with a true scope and spirit of the invention being indicated by the following claims.

The subject matter described herein may be embodied in other specific forms without departing from the spirit or essential characteristics thereof. The foregoing embodiments are therefore to be considered in all respects illustrative rather than limiting. While embodiments are susceptible to various modifications, and alternative forms, specific examples thereof have been shown in the drawings and are herein described in detail. It should be understood, however, that the invention is not to be limited to the particular forms or methods disclosed, but to the contrary, the invention is to cover all modifications, equivalents, and alternatives falling within the spirit and scope of the various embodiments described and the appended claims. Any methods disclosed herein need not be performed in the order recited.

11

The methods disclosed herein include certain actions taken by a practitioner; however, they can also include any third-party instruction of those actions, either expressly or by implication. For example, actions such as “identifying a target region of skin tissue” include “instructing the identification of a target region of skin tissue.”

The ranges disclosed herein also encompass any and all overlap, sub-ranges, and combinations thereof. Language such as “up to,” “at least,” “greater than,” “less than,” “between,” and the like includes the number recited. Numbers preceded by a term such as “about” or “approximately” or “substantially” include the recited numbers. For example, “about 3 mm” includes “3 mm.” The terms “approximately,” “about” and/or “substantially” as used herein represent an amount or characteristic close to the stated amount or characteristic that still performs a desired function or achieves a desired result. For example, the terms “approximately,” “about,” and “substantially” may refer to an amount that is within less than 10% of, within less than 5% of, within less than 1% of, within less than 0.1% of, and within less than 0.01% of the stated amount or characteristic.

EXAMPLES

Modern nanoparticle synthesis techniques have enabled the development of materials with unique optical properties for a wide range of applications including diagnostic, obscurant, and therapeutic applications. When as-fabricated nanoplates are concentrated using tangential flow filtration, the shape many of the plates shift to nanospheres, reducing the formulation efficacy, as evidenced by the increased peak height at 400 nm. By exchanging the surface capping agent of as-fabricated silver nanoplates with an agent that provides stability before, during, and/or after concentration, the silver nanoplates can be concentrated to increase the solution optical density without destabilizing the plates and degrading the beneficial optical properties.

The description of specific examples below are intended for purposes of illustration only and are not intended to limit the scope of the invention disclosed herein.

Example 1

15 L of silver nanoplates with a peak optical density of about 5 cm^{-1} were mixed with 3.5 g of polyvinylalcohol (PVA), and concentrated using tangential flow filtration using a 500 kD polysulfone tangential flow membrane with 3100 cm^2 of surface area. The solution was concentrated for approximately 90 minutes, and the final solution volume was reduced from 15 L to 0.5 L. The increase of the silver nanoplate solution optical density was from 5 to about 150 cm^{-1} . Thus, according to one embodiment, a method for increasing a silver nanoplate solution from 5 cm^{-1} to 150 cm^{-1} (e.g., an increase of roughly 30 times the optical density) comprises the steps of adding PVA to silver nanoplates, and concentrating the solution with tangential flow filtration.

Example 2

1.2 L of silver nanoplates with a peak optical density of about 4 cm^{-1} were mixed with 4 L of anhydrous ethanol and about 49 mL of ammonium hydroxide solution. 0.6 mL of a dilute aminopropyltriethoxysilane (APTES) was added to the solution. After 15 minutes of incubation, 6.5 mL of tetraethylorthosilicate (TEOS) solution was added. After 24 hours 1 L of the solution was concentrated using a 500 kD polysulfone tangential flow membrane with 1050 cm^2 of surface area. The

12

final solution volume was decreased to 150 mL, increasing the silver nanoparticle solution optical density to about 40 cm^{-1} . Thus, according to one embodiment, a method for increasing a silver nanoplate solution from 4 cm^{-1} to 40 cm^{-1} (e.g., an increase of roughly 10 times the optical density) comprises the steps of adding anhydrous ethanol, ammonium hydroxide solution, aminopropyltriethoxysilane (APTES), and tetraethylorthosilicate (TEOS) to the silver nanoplates, and concentrating the solution with tangential flow filtration.

Example 3

A 40 mL solution of 40 O.D. solution of concentrated silver nanoplates was spun at 3000 RCF for 30 minutes. This processed was used to concentrate the silver nanoplates to an optical density of 1000 O.D.

Example 4

A 5 mL solution of 1000 OD silver nanoplates was added to a 3"×3" section of absorbant cloth (Absorber Synthetic Drying Chamois, Clean Tools). After addition, the substrate was allowed to air dry. Once dried, the silver nanoplates were bound to the surface of the absorbant cloth and were not released when the cloth was subsequently wet and water removed by applying pressure.

REFERENCES

- Aherne, D. L., D. M.; Gara, M.; Kelly, J. M., 2008: Optical Properties and Growth Aspects of Silver Nanoprisms Produced by Highly Reproducible and Rapid Synthesis at Room Temperature. *Advanced Materials*, 18, 2005-2016.
- Chen, S., and D. L. Carroll, 2003: Controlling 2-dimensional growth of silver nanoplates. *Self-Assembled Nanostructured Materials Symposium (Mater. Res. Soc. Symposium Proceedings Vol. 775)*, 343-348/xiii+394.
- Chen, S. H., and D. L. Carroll, 2002: Synthesis and characterization of truncated triangular silver nanoplates. *Nano Letters*, 2, 1003-1007.
- Chen, S. H., and D. L. Carroll, 2004: Silver nanoplates: Size control in two dimensions and formation mechanisms. *Journal of Physical Chemistry B*, 108, 5500-5506.
- Chen, S. H., Z. Y. Fan, and D. L. Carroll, 2002: Silver nanodisks: Synthesis, characterization, and self-assembly. *Journal of Physical Chemistry B*, 106, 10777-10781.
- Hao, E., G. C. Schatz, and J. T. Hupp, 2004: Synthesis and optical properties of anisotropic metal nanoparticles. *Journal of Fluorescence*, 14, 331-341.
- Hao, E. K., K. L.; Hupp, J. T.; Schatz, G. C., 2002: Synthesis of Silver Nanodisks using Polystyrene Mesospheres as Templates. *J Am Chem Soc*, 124, 15182-15183.
- He, X. Z., X.; Chen, Y.; Feng, J., 2008: The evidence for synthesis of truncated silver nanoplates in the presence of CTAB. *Materials Characterization*, 59, 380-384.
- Jin, R., Y. Cao, C. A. Mirkin, K. L. Kelly, G. C. Schatz, and J. G. Zheng, 2001: Photoinduced Conversion of Silver Nanospheres to Nanoprisms. *Science*, 294, 1901-1903.
- Jin, R., Y. C. Cao, E. Hao, G. S. Metraux, G. C. Schatz, and C. A. Mirkin, 2003: Controlling anisotropic nanoparticle growth through plasmon excitation. *Nature*, 425, 487.
- Le Guevel, X. W., F. Y.; Stranik, O.; Nooney, R.; Gubala, V.; McDonagh, C.; MacCraith, B. D., 2009: Synthesis, Stabilization, and Functionalization of Silver Nanoplates for Biosensor Applications. *J Phys Chem C*, 113, 16380-16386.

13

Metraux, G. S. M., C. A.; 2005: Rapid Thermal Synthesis of Silver Nanoprisms with Chemically Tailorable Thickness. *Advanced Materials*, 17, 412-415.

Xiong, Y. J., A. R. Siekkinen, J. G. Wang, Y. D. Yin, M. J. Kim, and Y. N. Xia, 2007: Synthesis of silver nanoplates at high yields by slowing down the polyol reduction of silver nitrate with polyacrylamide. *Journal of Materials Chemistry*, 17, 2600-2602.

Xue, C. M., C. A., 2007: pH-Switchable Silver Nanoprism Growth Pathways. *Angew Chem Int Ed*, 46, 2036-2038.

Each of the references listed above is incorporated by reference in its entirety.

What is claimed is:

1. A process for increasing an optical density of a solution of stable, silver nanoplates to preserve shape post-concentration, comprising:

providing a solution comprising silver nanoplates having a plate shape, an extinction spectra, and a first peak optical density between $0.1-10\text{ cm}^{-1}$;

adding a concentration stabilizing chemical agent to the solution of silver nanoplates;

adding borate to the solution of silver nanoplates; and increasing the concentration of silver nanoplates in the solution to generate a concentrated solution using tangential flow filtration, thereby increasing the optical density of the concentrated solution to a second peak optical density greater than 10 cm^{-1} ,

wherein the silver nanoplates in the concentrated solution retain the plate shape and the extinction spectra at the second peak optical density greater than 10 cm^{-1} .

2. The process of claim 1, wherein the stabilizing agent comprises at least one of the group consisting of polyvinyl pyrrolidone, polyvinyl alcohol, polyethylene glycol, and dextran.

3. The process of claim 1, wherein the stabilizing agent comprises at least one of the group consisting of polysulphonates, ethylene oxides, phenols, and carbohydrates.

4. The process of claim 1, wherein the concentration stabilizing chemical agent is a water soluble polymer.

5. The process of claim 1, wherein the concentration stabilizing chemical agent is a metal or metalloid oxide.

6. The process of claim 5, wherein the stabilizing chemical agent is a silicon dioxide shell.

7. The process of claim 6, wherein the silicon dioxide shell ranges in thickness from 1 nm to 100 nm.

8. The process of claim 5, wherein the stabilizing chemical agent is a titanium dioxide shell.

9. The process of claim 1, wherein a combination of stabilizing agents are used.

14

10. The process of claim 1, further comprising adding any of the group selected from an acid, a base, and a buffering agent to the solution.

11. The process of claim 1, wherein the silver nanoplates have an aspect ratio of between 1.5 and 25.

12. The process of claim 1, wherein the silver nanoplates have an edge length between 10 nm and 250 nm.

13. The process of claim 1, further providing the solution of silver nanoplates with a seed mediated growth method.

14. The process of claim 1, wherein the concentrated solution of silver nanoplates is washed with between 1 and 5 wash volumes after increasing the concentration using tangential flow filtration.

15. The process of claim 1, where the solution of silver nanoplates is incubated with a substrate.

16. A process for increasing an optical density of a solution of stable silver nanoplates to preserve shape post-concentration, comprising:

providing a solution comprising silver nanoplates having a plate shape,

wherein the solution has an extinction spectra and a first peak optical density between $0.1-10\text{ cm}^{-1}$;

adding a polyvinyl containing polymer and borate to the solution; and

increasing the concentration of silver nanoplates in the solution to generate a concentrated solution, thereby increasing the optical density of the concentrated solution to a second peak optical density greater than 10 cm^{-1} ,

wherein the silver nanoplates in the concentrated solution retain the plate shape and the extinction spectra at the second peak optical density greater than 10 cm^{-1} .

17. The process of claim 16, wherein silver nanoplates have an individual edge length between 10 nm and 250 nm and an aspect ratio of between 1.5 and 25, and wherein the polyvinyl containing polymer comprises any one or more of the group consisting of: a polyvinyl alcohol and polyvinyl pyrrolidone.

18. The process of claim 16, further comprising adding any one or more of the group consisting of: an acid, a base, and a buffering agent to the solution.

19. The process of claim 16, further comprising providing via seed mediated growth the silver nanoplates with an aspect ratio of between 1.5 and 25 and associating the solution with a substrate.

20. The process of claim 16, further comprising associating the silver nanoplates with skin.

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